SciencePG
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Review Article

Selenium in Animal Nutrition: Deficiencies in Soils and Forages, Requirements, Supplementation and Toxicity

Uttam Saha[1], Abioye Fayiga[3, *], Dennis Hancock[2], Leticia Sonon[1]

[1]Agricultural and Environmental Services Laboratories, University of Georgia Cooperative Extension, Athens, Georgia, USA

[2]Department of Crop and Soil Science, University of Georgia, Athens, Georgia, USA

[3]Freelancer, Ibadan, Nigeria

Email address:

abioyeg@aol.com (A. Fayiga)

*corresponding author

Abstract: Selenium (Se), an essential nutrient for animals and humans, occurs as selenoproteins in enzymes. It is very important in animal nutrition because it functions as an anti-oxidant assisted by vitamin E. Se deficiency is a major problem which can be reduced or prevented by supplementation with inorganic or organic sources of Se. However, excessive supplementation and consumption of Se accumulating plants may lead to Se toxicity and animal poisoning. Minimal lethal dose for animals range between 1.5 to 8 mg kg^{-1} Se live body weight and maximum tolerable concentration of Se in forages is 5 mg kg^{-1}. Se deficiency in animals also depends greatly on Se content of forages and soils. Se deficient soils contain less than 0.6 mg kg^{-1} and can be fertilized to increase Se content of forages or pastures for animals. Forages are classified as adequate, marginally deficient and deficient in Se and contain 0.2, 0.1-0.199 and <0.1 mg kg^{-1} Se respectively. Silages can also be fortified with selenium to meet the requirements for Se in animals. The requirements of Se for animals need to be met to provide adequate animal and human nutrition.

Keywords: Selenium, Forages, Selenium Supplementation, Selenium Deficiency, Anti-oxidant, Selenium Toxicity

1. Introduction

Selenium (Se) is one of the 103 known chemical elements (like oxygen, hydrogen, carbon and others); it was discovered by the Swedish chemist Berzelius in 1817 (Rayman, 2000). According to animal nutritionists, Se was first known as an essential nutrient through the research work of Schwarz and Foltz (1957). However, its importance in animal diets was reported in 1941 (Leo, 1999) through the experimental evidence published by Poley et al. (1941) where they observed faster growth of chicks fed a diet with 2 ppm Se composed of an appropriate combination of seleniferous grains corn, barley and wheat grown in Se-rich soils of South Dakota.

In 1973, the selenoprotein called glutathione peroxidase (GSHpx) was first identified as an enzyme containing Se as its structural component (Rotruck et al., 1973; Hefnawy and

Tórtora-Pérez 2010). There are eight forms of GSHpx which are characterized by similar features, different modes and sites of action and different chemical forms (Mehdi et al., 2013). Other knownselenoproteins or enzymes where Se exists as a structural component are deiodinases, thioredoxin reductases, selenophosphate synthatase, selenoprotein P, selenoprotein W etc (Köhrle, 2000; Behne and Kyriakopulos, 2001).

Although, 30 selenoproteins have been identified in recent years, 25 are known to exist in humans and mammals (Thomson, 2013; Mehdi et al., 2013). In particular, the extremely vital role of the GSHpx enzyme system in animal and human physiology and health established Se as a unique essential micronutrient in animal and human diets. On the other hand, we also know that Se is toxic to human and animal health when its intake is too high. Because Se is an essential nutrient that can also be toxic at high levels, it is important to

ensure that the range of Se concentration in the animal diet is appropriate (Handa et al., 2016). Long-term exposure to Se has resulted into chronic poisoning of livestock and humans from areas with high levels of selenium in the soil (Alexander, 2015). The availability of Se in the soil and forage greatly affects animal nutrition and health. There is a need to meet the requirements of Se for animals in regions with deficient soils and forages since Se is very important for animal and human nutrition.

The goal of this paper is to provide a review on nutritional importance of Se and the status of Se in soils and forages with regard to meeting requirements of Se for animals. This is important because adequate animal nutrition often leads to adequate human nutrition in regions where animals provide the main protein source. This paper highlights the unique role of Se in animal nutrition, its concentration and distribution in soils and forages, its deficiency, supplementation, and toxicity disorders.

2. Importance of Selenium

2.1. Role as Anti-oxidant

In both human and animal physiology, a normal metabolic process called oxidation breaks down (or burns) carbohydrates, fats, and proteins of foods or feeds producing carbon dioxide, water, and energy. The energy produced via this process is utilized in various body functions (such as work, weight gain, milk production etc). However, oxidation of body's structural (e.g., cell membranes) and functional (e.g., enzymes and intracellular substances) components is very harmful. A simple analogy is that although gasoline is burnt to propel a car, it is protected so that the car's components do not burn.

The body must also have a defence mechanism to protect its components from oxidation-induced damage. This defence is provided by an antioxidant defence mechanism or simply antioxidant activity. Water is produced via reduction (reduction is a process opposite to oxidation) of molecular oxygen. The process of sequential reduction of molecular oxygen to water leads to formation of the following reactive oxygen species (ROS) in sequence; superoxide anion(which is both ion and radical), peroxide (hydrogen peroxide; organic peroxides) and hydroxyl radical(the most reactive of them all).

In addition to ROS, breakdown of proteins results in the formation of nitrogen free radicals (NFRs). For example, nitric oxide (NO) is an NFR produced during the transformation reaction of arginine (an amino acid) and oxygen to form citrulline (another amino acid). Nitric oxide and the product of its reaction with the superoxide O_2^-) anion, called peroxynitrite (ONOO−), both can cause cell damage in two different ways.

Both ROS and NFRs are powerful oxidizing agents. If ROS and NFR are not destroyed, they damage living cells, notably their proteins, lipids (fat), and nucleic acids (e.g., DNA). Unsaturated fatty acids which are the major component of all cell membranes are particularly susceptible. Their oxidation

by ROS results in the formation of lipid hydroperoxides (organic peroxides), which is quite damaging (called oxidative damage). Membranes particularly at risk of such damage include those in mitochondrial, red blood, and gastrointestinal cells (Behne and Kyriakopulos, 2001). Many selenoproteins are antioxidant enzymes that participate in maintaining cell redox balance (Zeng et al., 2013).

The GSHpx family of selenoproteins (or enzymes) helps to prevent the formation of ROS and NFR. Using glutathione as a reductant, they also catalyze the reduction of the hydrogen peroxide (convert it to water) and lipid hydroperoxides (convert them to lipid alcohols), thus preventing oxidative damage and ensuring cell membrane integrity (Hoekstra, 1974; Wendel, 1980). Since Se is an integral component of the intracellular enzymes, GSHpx, an adequate level of Se in animal body is essential for a proper level of GSHpx. In Se deficiency, marked decreases in the activity of GSHpx and other Se-dependent enzymes contribute to lowered defences against oxidative damage (Hornsby et al., 1985; Burk, 1990).

Se can also act as a proxidant (Hasanuzzaman et al., 2010). Pro-oxidant activity is the antonym of antioxidant activity; sodium selenite and some other inorganic Se compounds such as Se dioxide and diselenides have such activity to catalyze the oxidation of thiols such as glutathione with a concomitant production of superoxide and other reactive oxygen species (Spallholz, 1997). This catalytic reaction of inorganic Se with thiols likely accounts for Se toxicity to cells in the major glutathione producing organs, such as the liver (Spallholz, 1997).

The pro-oxidant influence of sodium selenite in animals (Spallholz, 1997) is of particular concern when shelf life of the produced milk, meat and egg is considered (Mahan, 2001; Surai et al., 2008). The pro-oxidant property of inorganic Se may also enhance multiplication of some pathogenic viruses. Sodium selenite can interact chemically with vitamin C (ascorbic acid) in the premix and the chemical reaction between them causes reduction of selenite to elemental Se (it often appears as pink particles in the premixes) and oxidation of vitamin C.

The elemental Se is not absorbed in the digestive tract (hence it is excreted) and oxidized vitamin C is devoid of biological activity (Eisenberg, 2007). Therefore, nutritional benefits of both Se and vitamin C are lost. The reduction of selenite to elemental Se could happen in the premix/feed during storage or even in the digestive tract during digestion and absorption. Some other components in the premix like glucose monohydrate, corn starch or sucrose can reduce selenite to elemental Se in the same way (Groce et al., 1973).

2.2. Interaction of Selenium with Vitamin E and Other Nutrients

There are several vitamins, including vitamin E, that are important in human and animal nutrition. Some vitamins are soluble in water whereas some others are soluble in fat (or lipid). As discussed above, animals must have an antioxidant defence mechanism to protect them from harmful oxidative damage. Both Se and vitamin E reduce oxidative damage as

follows: first, vitamin E blocks ROS attacks on lipids and reduces the formation of lipid hydroperoxides; Se being apart of GSHpx, prevents the formation of ROS and destroys (via reduction) hydrogen peroxide and lipid hydroperoxides. Thus the occurrence and extent of oxidative damage depends on the antioxidant protective mechanisms of the lipid-soluble vitamin E that is present in the cell membrane and the level of water-soluble Se–containing GSHpx in the aqueous fluid within the cells.

Therefore, any discussion of Se needs to also include vitamin E because of their interrelated functions. An inadequate amount of Se or vitamin E in the diet results in similar adverse effects of increased oxidative damage, making either of them useful to treat or alleviate these adverse effects. Moreover, the amount of Se or vitamin E needed by the animal depends on the availability of the other as illustrated in Figure 1.
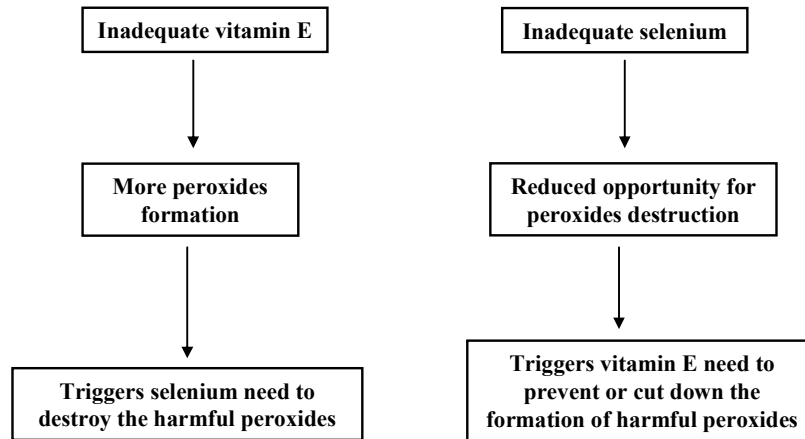
Figure 1. *Interactive need of vitamin E and Se in animal and human diet.*

Optimum amounts of both Se and vitamin E, however, are necessary to minimize oxidative damage. Surai et al. (2016) reported that increased supplementation of the maternal diet substantially increased concentrations of vitamin E and Se in developing chick tissues and significantly decreased susceptibility to lipid peroxidation. Thus, both Se and vitamin E should be considered together with regard to the animal's requirements; and with regard to the effects and treatment of a deficiency of either. The level of dietary selenium needed to prevent deficiency depends on the vitamin E status and species of the host (Fordyce, 2013). Vitamin E and Se supplementation has been shown to either increase or have no effect on milk production in cow and sheep (Tufarelli, 2011). Se plus vitamin E significantly increased the incidence of oestrus, fertility and body weight of lambs (Koyuncu and Yerlikaya, 2007).

Recently, a study was conducted to evaluate the effects of 2 dietary Se sources and 2 vitamin E levels during gestation and lactation on antioxidant status and reproductive performance in multiparous sows. α-tocopherol, a form of vitamin E is found in the greatest amounts in blood and tissues of humans (Beck, 2007). The α-tocopherol level in serum increased when sows were fed elevated vitamin E diets and no vitamin E treatment or Se source × vitamin E level interaction was evident for reproductive performance and the indices measured in serum and milk (Chen et al., 2016).

A number of additional substances also have antioxidant activity and, therefore, can decrease vitamin E and Se needs when their intake is high. They can also increase vitamin E and Se needs when their intake is low. These include: the sulfur containing amino acids cysteine and methionine, vitamin C, and synthetic antioxidant ethoxyquin, which is commonly added to commercially prepared feed.

Certain mineral nutrients affect the absorption and metabolism of Se and hence can alter the dietary Se requirement. These include calcium (Ca), sulfur (S) and copper (Cu). The apparent digestibility and absorption of Se is reduced when cows are fed diets with both high (around 1.4%) and low (around 0.4%) concentrations of calcium (Harrison and Conrad, 1984) thereby increasing the requirement of dietary Se. The Se absorption was, however, maximum when dietary calcium was 0.8% (Harrison and Conrad, 1984).

A positive relationship between dietary levels of copper and Se absorption has been reported in sheep (White et al., 1989; Hartmann and van Ryssen 1997) but not in dairy cows (Koenig et al., 1991). A study on the effects of Se, S, and Cu levels on selenium concentration in liver and serum of lambs revealed an antagonist effect of S and Cu on Se absorption in the animals (Netto et al., 2014). A three-way interaction and a reduction of Se concentration was verified when Cu and S concentrations were increased (Netto et al., 2014). The antagonism effect of both S and Cu on Se may be partly due to high dietary sulfur which reduces Cu absorption probably via formation of copper sulphide (Spears, 2003).

3. Selenium in Animal Nutrition

3.1. Selenium and Sulfur

Chemically, both Se and S are members of Family VI of the periodic table and they have many common physical and chemical properties. Because of these similarities, they are called chemical analogs of each other; and can replace each other. Upon intake, Se replaces S of some organic metabolites.

Methionine is a S containing essential amino acid in animal nutrition (i.e., animals cannot synthesize it and hence it should come from plant materials fed to animal), Se can replace its S component to a large extent forming selenomethionine (SeMet) and seleno-methyl-selenomethionine. Other selenoamino acids like selenocysteine, and seleno-methyl-selenocysteine can also form via replacement of S in the amino acid, cysteine.

The SeMets are integral part of the enzymes GSHpx, the primary source of antioxidant activity in the animal body. However, under excessive intake of S, replacement of S by Se in methionine (or other S containing metabolites) and formation of SeMet becomes difficult due to competitive action of S. That means actual absorption of Se decreases and excretion increases. Thus the addition of sodium sulfate to the diet of pregnant ewes (total dietary S = 0.33%) increased the incidence of white muscle disease in their lambs (Hintz and Hogue, 1964).

Holstein steers grazing S fertilized herbage had lower blood GSHpx activity than those grazing unfertilized herbage (Murphy and Quirke 1997). Within forages, legumes promote greater incidence of white muscle disease than grasses (Whanger et al., 1972), which is due to high S contents of legumes and the presence of cyanogenic glycosides (Gutzwiller, 1993). But these attributes of legumes can be useful to counteract the Se toxicosis as discussed later.

Plants cannot distinguish between these S and Se while synthesizing amino acids because they are chemical analogs. As a result they can synthesize the selenoaminoacid called selenomethionine (SeMet) instead of methionine(a S containing amino acid) when Se is available. This biological feature was the basis for development of the commercial technology of organic Se-enriched yeast.

Plants absorb Se from soil predominantly in the inorganic forms of selenate or selenite and utilize them primarily in the synthesis of SeMet via replacement of sulfur with Se in methionine (Schrauzer, 2003; Surai et al., 2008). Other selenocompunds like seleno-methyl-selenomethionine, selenocysteine, and seleno-methyl- selenocysteine can also form, but SeMet represents more than 50% of the Se in small grains (Olsen and Palmer, 1976). It is also the major selenocompound in other cereal grains, forage legumes, and soybeans (Whanger, 2002).

However, in Se rich food plants such as garlic, onions, broccoli florets and sprouts, and wild leeks, *seleno-methyl-selenocysteine* is the major selenocompound (Whanger, 2002). In forage plants, storage of SeMet in leaves is 1.5 to 2 times more than that in stems (Gupta and MacLeod, 1994). When grown on low Se soils, seeds and vegetative parts generally have similar concentrations of Se, but as the Se in soil increases, the Se concentration in seeds and roots become higher than that in stems and leaves (Harada et al., 1989; Stephen et al., 1989; Schrauzer, 2003).

Increased consumption of S (from sulfate salt) has been reported to be associated with reduced Se absorption thereby increasing the requirement of dietary Se in sheep (Pope et al., 1979) and lactating dairy cows (Ivancic and Weiss, 2001) but not in non-lactating cows (Gant et al., 1998) or beef cattle (Khan et al., 1987). Excessive intake of feeds that are high in S such as, molasses, beet pulp, cruciferous plants, and corn-distilling by products such as corn gluten feed (Hale and Olsen, 2001) may aggravate Se deficiency even when Se level in the diet is adequate.

3.2. Selenium Deficiency

The most commonly manifested clinical sign of Se deficiency is called white muscle disease (or nutritional myopathies) which results in degeneration and necrosis in both skeletal and cardiac muscle (Underwood and Suttle, 2001). This may be congenital or delayed. Se deficiency can affect reproduction in a cow herd via increasing the incidence of early embryonic death and retained placentas. A more detailed listing of Se deficiency signs in ruminants and non ruminants (i.e., monogastric animals) are given in Figure 2.
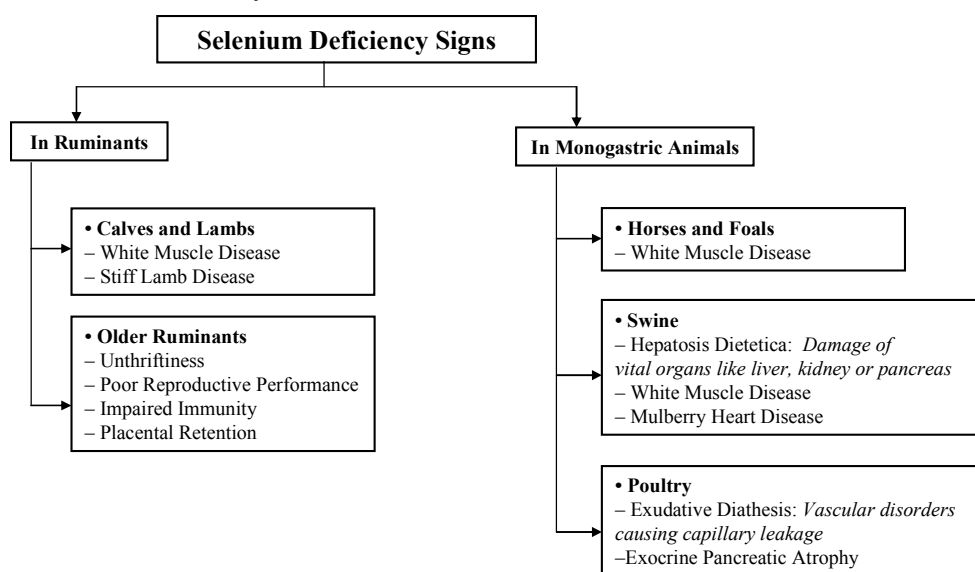

Figure 2. Selenium deficiency signs in various animals.

Selenium status in soil, plants and animal blood and tissue can be used in the diagnosis of Se deficiency (Hefnawy and Tórtora-Pérez, 2010). Clinically, one of the most effective ways to diagnose Se deficiency is by determining the Se concentration in the liver. Liver levels of 0.8-1.0 ppm on wet weight basis are considered to be adequate, and levels below 0.2 ppm are considered to be deficient. Another method for determining Se status is to determine the activity of erythrocyte GSHpx; it is especially helpful in suspected cases of long-term Se deficiency. As a general indicator of potential Se deficiencies, whole blood samples can be utilized. Concentrations of 0.05 ppm and below are considered to be deficient.

In ruminants, sheep are more susceptible than cattle to Se deficiency (Muth, 1963; Grace, 1994) and goats are more susceptible than lambs or calves (Rammel et al., 1989). Sudden deaths of the largest, fastest growing animals in commercial operations are commonly attributed to Se and/or vitamin E deficiency. The incidence of highest occurrence seems to be largely in areas of the United States where the forages and grains are low in Se, suggesting that the indigenous Se in forages and grains is important in preventing Se deficiency disorders in animals (Mahan, 2001).

Clinical and subclinical signs of Se deficiency have been reported in beef cows and calves receiving forages containing 0.02 to 0.05 mg Se per kg (Morris et al., 1984; Hidiroglou et al., 1985; Spears et al., 1986). Based on a limited scale survey of the state veterinarians and state veterinary diagnostic laboratories for Se deficiency and toxicosis in animals, Edmondson et al. (1993) reported Se deficiency as major problems in regions of 37 states which did not include Georgia. However, Georgia was categorized as a state of mild Se deficiency (Edmondson et al., 1993), which often remains hidden without any diagnostic sign. This is certainly damaging to animal performance and it causes substantial loss in revenue of livestock operations in the state, but it is yet to be fully realized and assessed.

Feeding diets rich in unsaturated or rancid fats may result in higher incidence of Se deficiency disorders than when animals are fed with normal diets (Ewan et al., 1969). Rancidification is the decomposition of fats, oils and other lipids by hydrolysis or oxidation, or both. Hydrolysis splits fatty acid chains away from the glycerol backbone in glycerides. These free fatty acids can then undergo further auto-oxidation. Oxidation primarily occurs with unsaturated fats by a ROS-mediated process.

3.3. Selenium Requirement

The dietary Se requirements for different classes of animals as recommended by the National Research Council (NRC, 1994; 1998; 2000; 2001; 2007; Lewis, 1995) are given in Table 1. Note that under specific situations, the actual Se requirement may be higher than what has been cited in the Table 1. For example, nutrient oxidation for energy needs increases with exercise, which increases the production of

ROS, thereby increasing the Se needed by the additional GSHpx required for removing the extra ROS produced (Lewis, 1995).

Similarly a higher desired level of weight gain or milk production may also raise the dietary Se requirement, which can be estimated utilizing appropriate equations (NRC, 2007). However, even though calculation of dietary Se requirements, based on appropriate equations, for a desired level animal performance may often turn out to be higher than what has been presented in Table 1, it is important to comply with the pertinent regulations of the Food and Drug Administration (FDA, 1997; 2004; 2005) which does not allow Se supplementation more than 0.3 mg kg-1 complete diet.

Table 1. *Recommended levels of Se in various animal diets.*

Animal	Se Requirements (mg/kg diet)
Beef Cattle	0.10
Dairy Cattle	0.30
Sheep	0.10-0.20
Growing Pigs	0.15-0.30
Gestating and Lactating Sows	0.15
Horse	0.10
Immature Laying Chickens	0.10-0.15
Laying Hens	0.05-0.08
Broiler Chicks	0.15

(NRC, 1994; 1998; 2000; 2001; 2007; Lewis, 1995).

3.4. Selenium Supplementation

Because feedstuffs (e.g., grains and forages) produced in many areas of the United States, including Georgia, are either deficient or at least marginally deficient in Se for desired animal functions, Se supplementation is required. The current pertinent regulation allows inorganic and organic sources of Se supplementation in livestock operations (FDA, 2004):

Inorganic supplements such as sodium selenite and sodium selenate are recommended and are more or less equally effective, but because of its lower cost, sodium selenite is commonly used. Sodium selenite is absorbed in the animal body passively via diffusion from the intestinal tract (Schrauzer 2000). Recently, it has been shown that DL-SeMet can replace sodium selenite in the diet of weaning pigs because it significantly improved the growth performance, antioxidant ability and plasma Se content (Cao et al., 2014).

The supplements can be supplied through diet, direct injection or oral drenching and by ruminal placement. Selenium intake in the diet can be increased by using Se rich feed ingredients or by providing selenized mineral supplements. The FDA permits manufactured premixes to contain Se of no more than 200 mgkg[-1] and mineral supplements to contain Se not exceeding 11.8 mgkg[-1]. The total diet of Se should not exceed 0.3 mg kg^{-1} and total desired supplement should not be over 3 mg/head/day. This level can, however, be supplemented to diets regardless of the natural Se indigenous in the feedstuffs.

Sodium selenite solution can be used as an intramuscular or subcutaneous injection or periodic oral drench at 0.1 mg Se per kg live body weight (LBW) for grazing animals (Meneses et al., 1994) that are not provided other concentrate feeds. The suggested application intervals are 1-3 months for small ruminants, every 3-4 months or during the critical production stages for beef and dairy cattle.

Kuchel and Buckley (1969) developed a heavy pellet of elemental Se and iron filings that was heavy enough to stay in the reticulum of rumen (forestomach) of ruminant animals. This pellet slowly dispenses Se over extended periods of time. Experience with their use showed that these heavy pellets were effective for almost a year (Judson et al., 1991). Unfortunately this pellet is not yet approved for use in the United States. Slow release ruminal glass boluses that contain Se from sodium selenite can be retained in the rumen that release Se over a period of months (Campbell et al., 1990). Soluble glass boluses sometimes contained other nutrient essentials in addition to Se (Telfer et al., 1984). Another product is osmotic pumps that will accurately deliver 3 mg Se per day.

As an alternative to inorganic supplements, Se can also be provided as a natural organic Se-enriched yeast (e.g., Sel-Plex®, Altech, Inc, Nicholasville, KY), which was approved by FDA for use in the poultry industry (Federal Register, 2000; 2002). The organic Se yeast provides a cocktail of organic Se compounds (Kelly and Power, 1995), but SeMet is the primary component (over 50% of the total Se). Thus the Se composition of this product matches closely that found in most grains. The SeMet of Se-enriched yeast is readily available and actively absorbed from the intestine via a system which is technically called sodium-dependent methionine transport system (Spencer and Blau, 1962; Mahan, 1995). Biotransfer potential of Se from Se-enriched yeast to milk and foetus (via placental transfer) (Mahan, 2000) and retention of Se in meat are substantially higher than from sodium selenite (Mahan et al., 1999).

The FDA in 1974 approved inorganic Se as a feed supplement; and sodium selenite became the most commonly used Se supplement for poultry and other livestock (Leeson and Summers, 1991). This decision was ironic because the commonly used plant- and animal based feedstuffs contain Se almost exclusively as organic compounds commonly known as selenoaminoacids; SeMet is the predominant compound of this class (Levander, 1986; Edens et al., 2008). The reason for FDA's decision in 1974 about the use of inorganic Se as a feed supplement was probably based on its low cost and lack of information about SeMet. Problems associated with inorganic Se include inability to build and maintain Se reserves in the body resulting in a greater proportion of consumed inorganic Se being excreted; low efficiency of Se transfer to milk, meat and egg; and potential toxicity via pro-oxidant activity, if the dietary supplementation is too high.

In a recent study, Se-Met was able to influence immunity at birth and 7 days of age while selenite did not improve the performance and immunity of goats. Even though Se concentrations significantly increased in the serum of kids of treated goats, colostrums and daily milk production were not affected by Se supplementation (Kachuee et al., 2013). The impact and results of Se supplementation in cattle depend on physiological stage, Se status of animals, type and content of Se and types of Se administration (Mehdi and Dufrasne, 2016).

4. Supplying Selenium in Soils and Forages

4.1. Selenium in Soils

The Se content of most soils varies between 0.1 and 2 mg kg^{-1} (Swaine, 1955). The maximum reported soil Se content in USA is less than 100 mg kg^{-1} (NRC, 1983). High Se soils or seleniferous soils with 2 to 10 mg kg^{-1} Se occur in South Dakota, Montana, Wyoming, Nebraska, Kansas, Colorado, and New Mexico. Depending upon soil properties and climatic conditions, a variable portion of the total soil Se is available to the vegetation under different situation. Thus, seleniferous soils are further divided into two different classes: toxic and non-toxic seleniferous soils.

Toxic seleniferous soils supply sufficiently available Se to produce vegetation with toxic level of Se for livestock. These soils are usually alkaline (pH >7.0) in reaction and occur in low rainfall regions with usually less than 8 inches total annual precipitation. Although the total Se content of nontoxic seleniferous soils is high, they yield insufficient Se for plants to be toxic. These soils are usually acidic (pH 4.5-6.5) in reaction, rich in iron and aluminium oxides and developed under humid conditions (Lakin, 1961)

Total Se content of many nontoxic seleniferous soils is significantly higher than that of some toxic seleniferous soils. For example, Hawaiian soils with total Se content 6-15 mg kg^{-1} do not produce vegetation containing toxic level of Se, whereas soils of South Dakota with a lower total Se content produce toxic plants (Lakin, 1961). Indeed it is the water soluble form of Se (not the total Se) in soils that is taken up by the vegetation to build up toxic quantities of the element (Lakin, 1972).

Soils containing 0.1 to 0.6 mg kg^{-1} total Se are classified as Se deficient soils (Umesh and Subhas, 2010). Regions that are Se deficient include New England, New York, New Jersey, Delaware, Pennsylvania, Maryland, West Virginia, Florida, Ohio, Indiana, Illinois, Michigan, Wisconsin, Washington State, Oregon, Montana, Arizona, and the coastal regions of Virginia, Carolinas, and Georgia (Cary et al., 1967; NRC, 1983).

4.2. Selenium in Forage

Although Se is not an essential element in plant nutrition, the consumption of plants and plant products is the primary avenue by which animals and humans receive their dietary intake of Se in the absence of any special supplementation (Ihnat, 1989). The level of Se in plants depends primarily on the water soluble Se (i.e., plant available Se) content of the soil.

According to Mortimer (1999), Se and other trace element contents of forage can be interpreted as deficient at the lowest level to Maximum Tolerable Concentration at the highest level presented in Table 2. Forage can be classified as adequate, marginally deficient, and deficient in Se when it contains around 0.2, 0.100-0.199, and <0.100 mg kg^{-1} Se. The Maximum Tolerable Concentration of Se in forage was around 2 mg kg^{-1} (NRC, 1980), which was subsequently increased to 5 mg kg^{-1} (NRC, 2005).

Table 2. Classification of trace elements in forage relative to their abilities to meet dietary requirements (Mortimer, 1999).

Element`	Deficient	Marginally Deficient	Adequate	MTC*
Aluminum (mg/kg)	-	-	-	1000
Copper (mg/kg)	<4	4-9.9	≥10	100
Iron (mg/kg)	<50	-	50-200	1000
Manganese (mg/kg)	<20	20-39.9	≥40	1000
Molybdenum (mg/kg)	-	-	<1	5
Selenium (mg/kg)	<0.100	0.100-0.199	0.200	2**
Sulfur (% DM)	<0.1		0.15-0.2	0.4
Zinc (mg/kg)	<20	20-29.9	≥30	500

*Maximum Tolerable Concentration DM-dry matter
** According to NRC (1980); the current MTC for Se is 5 mg/kg (NRC, 2005).

The Se levels in various forage crops as determined through a nationwide study of 709 samples from 678 producers from 23 cooperating states including 28 samples from Georgia is summarized in Table 3 (Mortimer, 1999). Although Se level apparently varied with the plant species, around 44 to 96% of the samples were either marginally deficient (0.100 to 0.199 mg/kg Se) or deficient (<0.100 mg/kg) in Se. Among the forage species, Fescue was notably deficient in Se; only 4% of the analyzed Fescue samples had Se levels adequate for animals. Almost none of the forage species had Se levels exceeding the Maximum Tolerable Concentration. Such results suggest that Se deficiency rather than toxicity is a concern in the samples included in the study of Mortimer (1999).
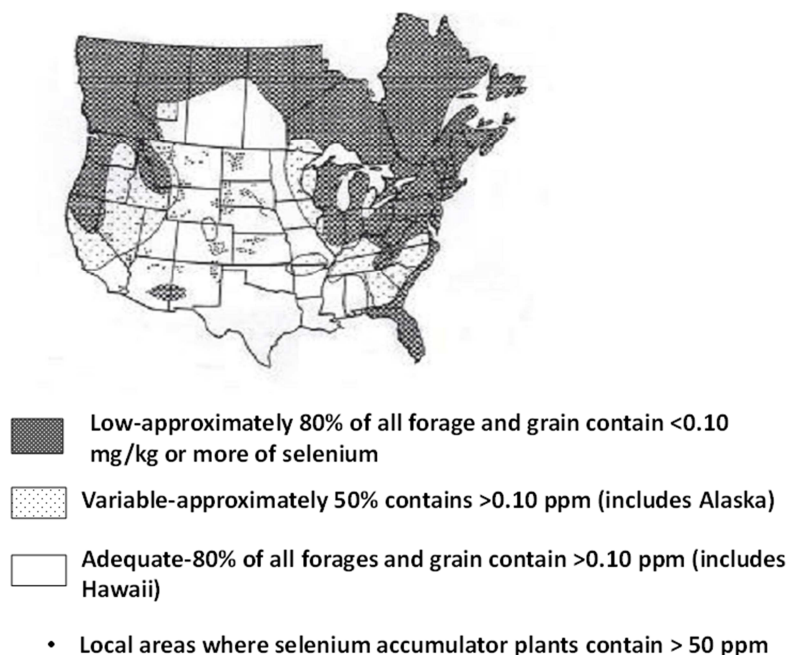
Table 3. Selenium content of forage samples.

Forage Type	Percentage of the analyzed samples under different Se levels*			
	Deficient	Marginally deficient	Adequate	>MTC**
Alfalfa/Alfalfa Mix	23.98	20.41	54.59	1.02
Brome	45.00	25.00	30.00	0.00
Bermuda	52.68	27.68	19.64	0.00
Fescue	78.08	17.81	4.11	0.00
Grass	48.57	28.57	22.86	0.00
Native grass	39.47	26.84	23.68	0.00
Orchard/Orchard grass mix	67.65	26.47	5.88	0.00
Sudan	31.15	45.90	22.95	0.00
Silage/Silage grass	32.26	22.58	45.16	0.00
Cereal	19.57	28.26	52.17	0.00
Other	42.86	17.86	42.86	0.00

*Based on the analyses of 709 forage samples from 678 producers from 23 cooperating states including 28 samples from Georgia (Mortimer, 1999).
**Maximum Tolerable Concentration.

Most cereal grains for livestock and human consumption are grown in areas with inadequate or moderate Se reserves (NRC, 1983). Forages and grains (or complete feed) containing less than 0.1 mg kg^{-1} Se may result in a Se/vitamin E deficiency disorder; a much higher incidence of this disorder occurs when the Se concentration drops below 0.05 mg kg^{-1}. The regional distribution of forages and grain, containing low, variable or adequate levels of Se in various areas of United States and Canada is shown in Figure 3 (NRC, 1983). Areas in the United States that produce grains and forages low in Se generally have soils that contain <0.5 mg/kg Se (Swaine 1955; Cary et al., 1967; Levesque 1974).

Low-approximately 80% of all forage and grain contain <0.10 mg/kg or more of selenium

Variable-approximately 50% contains >0.10 ppm (includes Alaska)

Adequate-80% of all forages and grain contain >0.10 ppm (includes Hawaii)

• Local areas where selenium accumulator plants contain > 50 ppm

Figure 3. Regional distribution of forage and grain Se content in the United States and Canada (NRC, 1983).

Liming acid soils, as well as adding Se to fertilizers have been used successfully to increase forage Se content and to prevent deficiencies in low Se areas (Gill and Rich, 1985; Varo et al., 1988). Fertilization with Se to produce Se enriched forages is an effective method to supplement animal diets in Se and improve animal growth and development (Hall et al., 2013; Chamheidar and Parvanak, 2014; Séboussi et al., 2016). Adding selenite or selenate to fertilizer has been shown to increase Se content of grain (Pond et al., 1971; Nielsen et al., 1979). Selenate is more effectively absorbed by plants than selenite (Koivistoinen and Huttenen, 1986). The Se content of silages is not enough to supply the Se requirement of cattle. Seppala et al. (2014) reported that addition of sodium selenate to silage additive provided a controlled way to add Se to the diet of forage fed animals. Application of Se-enriched fertilizer increased the Se concentration of hay to a level sufficient to meet the dietary requirement for horses (Montgomery et al., 2011).

Adding animal manure to cropland and pastures from animals fed supplemental Se (as selenite) may not result in increased plant Se content (CAST, 1994). This is because of the fact that Se (as selenite) fed to animal gets converted to a chemically reduced (i.e. selenide form) form in the intestinal tract and excreted in manure, most of which is not available for plant uptake. Whelan et al. (1994) reported that treating forage and pasture land with less soluble forms of barium selenate ($BaSeO_4$) at 10 g Se per hectare in granular form is effective for 3 years. However, we need research in this area in order to provide recommendations for effective management of animal nutrition.

Plant type (plant genetics) influences Se accumulation in plants. The primary and secondary accumulator plants (or indicator plants) have been found to grow in 140 counties in 16 states of the United States excluding Georgia (NRC, 1971).

Selenium concentration in plants can range from 0.005 mg kg^{-1} in deficient crops to more than 1000 mg kg^{-1} in Se accumulators on seleniferous soils (Umesh and Subhas, 2010). However, these plants probably add very little to Se content of feeds because they normally grow in dry non-agricultural areas (NRC, 1983). A classification of Se accumulator plants as given by Knight (1995) is presented in Table 4.

Table 4. Various kinds of Se accumulator plants (Knight, 1995).

Obligate Se accumulator or indicator plants	
Common name	**Genus/species**
Milk vetches	*Astragalus* (24 spp.)
Golden weeds	*Haplopappus* spp.
Wood asters	*Xylorrhiza glabriuscula*
Prince's plume	*Stanleya pinnata*
Secondary or facultative Se accumulator plants	
Common name	**Genus/species**
Asters	*Aster* spp. and *Machaeranthera* spp.
Saltbrush	*Atriplex* spp.
Indian paintbrush	*Castilleja* spp.
Broomweed	*Gutierrezia* spp.
Turpentineweed	Not available
Snakeweed or Matchweed	Not available
Beard tongue	*Penstemon* spp
Gumweed or Resinweed	*Grindelia squarrosa*
Ironweed	*Sideranthus grindelioides*
Bastard toadflax	*Comandra pallid*

The obligate Se accumulator plants grow only on soils high in available Se because they require a high amount of Se for their normal growth. These plants are capable of accumulating up to 10 times the amount present in the soil (called enrichment factor). Some may contain Se up to 10,000 mg kg^{-1} or 2000 times the maximum tolerable concentration (5 mg kg^{-1}, according to NRC, 2005) and thus may cause acute Se poisoning. In contrast to obligate accumulators, the secondary accumulator plants do not require Se for growth, but they may accumulate up to several

hundred mg kg^{-1} of Se when grown on soils high in available Se. The secondary Se accumulator plants may cause either acute or chronic Se poisoning depending on the amount ingested and the Se content (Knight, 1995).

As categorized by Knight (1995), the third group of plants which are used as livestock feed, are the crop plants, alfalfa and grasses. They may contain Se from 1 to 30 mg/kg, if grown on Se-rich soils. Fortunately, the high Se content of Se accumulator plants gives them an unpleasant garlic-sulfur odor, which makes them unpalatable to livestock and hence animals generally avoid eating them unless other feeds or forages are not available. This distinct featured odor assists in identifying their presence in the field; the odor is increased by rubbing their leaves together.

5. Selenium Toxicity

Historically, Se toxicity (called *selenosis*), rather than Se deficiency was the concern, which triggered extensive research on Se in animal nutrition (NRC, 2001). As we already know, a number of detrimental effects occur if the diet contains Se less than 0.1 mg kg^{-1}. However, amounts greater than 5 mg kg^{-1} Se in the diet is harmful and causes Se poisoning in livestock (Buck and Osweiler, 1976). Poisoning in livestock due to toxic levels of Se may be acute or chronic as discussed later. When excess Se intake takes place, the body itself attempts to get rid of excess Se through urine (e.g., as trimethylselenonium), bile and lungs (e.g., as volatile dimethyl selenide) or trapping it in various tissues (e.g., muscle, hair), making it biologically less available. The portion that overwhelms these excretion and trapping systems produces toxic effects.

There are reported cases of Se toxicity in grazing animals due to the consumption of Se accumulating plants. Many plant species of *Astragalus* and *Stanleya* when grown on seleniferous soil can accumulate Se up to 3000 mg kg^{-1} (NRC, 2000) as compared to 2-5 mg kg^{-1} which is the maximum tolerable concentration in forages (NRC, 1980; 2005). However, the unpleasant garlic-sulfur odor of the Se accumulator plants makes them unpalatable to livestock. Thus, acute selenosis from accumulator plants is generally not a practical problem because livestock usually avoid these plants, unless pastures are overgrazed or other forages are not available.

The main problems with excess Se are often due to excessive supplementation, which may results from errors in weighing Se premixes or administering injectable preparations exceeding the recommended limit. Misformulated supplement products were responsible for the most serious Se toxicity outbreak that has occurred in the U. S (Morris and Crane, 2013). In such cases, various acute toxicity signs are manifest or even death of the affected animal is not uncommon. Miller and William (1940) determined the minimum lethal doses of Se from sodium selenite (used for Se supplementation) for horses, cattle, and swine as 1.5, 4.5-5.0, and 6-8 mg Se kg^{-1} live body weight (LBW).

Responses to toxic level of Se or selenosis are characterized as acute (effects manifest within a short time period) or chronic (effects manifest over a long time period). Although the sub-acute exposure (62.5 μg Se/kg bw/ day; 14 days) to a relatively high concentration of Se causes an increase in concentration of some biomarkers of intracellular processes, especially in the brain, the effect of Se can be considered as low toxicity (Jansen et al., 2013). Acute selenosis can occur when cattle are fed 10 to 20 mg Se or injected ≥0.5 mg Se kg^{-1} LBW (NRC 1983; NRC 2001). In swine, acute selenosis occurs when Se is injected at ≥1.65 mg (Diehl et al., 1975) or fed at ≥20 mg kg^{-1} LBW (Mahan and Moxon, 1984). Acute Se poisoning associated with sudden death occurs due to pulmonary congestion and edema. Acute selenium intoxication is followed by adverse effects on the nervous system in humans (Vinceti et al., 2014).

Chronic selenosis has been reported to occur when diets or feedstuffs for swine contain Se at 5 to 20 mg kg^{-1} DM (Kim, 1999) or 5 to 40 mg kg^{-1} DM in both dairy and beef cattle (NRC, 2000; 2001) for a period of several weeks or months. The recommended dietary Se requirement (0.3 mg kg^{-1}) is approximately 16 times less than the lowest dietary level (5 mg kg^{-1}) that has been related to chronic selenosis. In chronic excess, Se profoundly inhibits cellular enzyme oxidation-reduction reactions, especially those involving sulfur-containing amino acids, methionine and cysteine, which affects cell division and growth (Rosenfeld and Beath 1964). These effects are greatest on hoof and hair, which are the body tissues that contain the highest concentrations of these amino acids. This manifests as clinical signs of abnormal hoof and hair conditions.

Laboratory animals (rabbits, rats and cats) receiving acute lethal doses of Se (≥3.0 mg kg^{-1} LBW) as sodium selenite or selenate developed a garlicky breath odor because of exhalation of volatile methylated Se metabolites; the primary volatile metabolite of this kind has been recognized as dimethyl selenide (Smith et al., 1937). Generally speaking, there is no effective way to counteract Se toxicity in livestock except to remove the animals from areas with high Se soils and close these areas to livestock production. Grains and forages in those areas, however, can still be used if they are blended with those from areas with low Se soils. The use of Se compounds with low potential for toxicity may be used to replace the highly toxic forms. For example, elemental Se at nano size (Nano-Se) is as equally efficient as Se-methylselenocysteine (SeMSC), a naturally occurring organic Se product with chemopreventive ability, but with reduced risk of Se toxicity (Zhang et al., 2008).

Linseed meal was used to protect animals from Se toxicity due to its content of the cyanogenic glycosides, linustatin and neolinustatin (Smith et al., 1980). Some reports demonstrated that selenosis may be counteracted by administering sodium arsenate (Moxon, 1937; 1941). Some other reports documented that organic arsenic compounds like 0.01% arsenilic acid and 0.005% 3-nitro-4-hydroxyphenylarsonic acid in the diet offered effective protection against toxic levels of Se (Wahlstrom et al., 1955; 1956) through chelating and diverting absorbed Se to the biliary system (Lavender and Bagman, 1966).

6. Conclusion

Selenium is a vital micronutrient in animal nutrition, required in trace quantity. At the same time, it exerts serious toxic consequences up to death when the intake exceeds the tolerance limit. Forages and grains used as animal feedstuffs are either deficient or marginally deficient in Se when they are grown on soils with low plant available Se content. Many areas of the United States fall in this belt. The geographical coincidence of Se deficiency in animals and low Se contents of the produced forages and grains (used as feedstuffs) in the United Sates suggests that the indigenous Se in forages and grains is important in preventing Se related health problems in animals. We believe that site specific application of Se as a fertilizer for forages and pastures may be needed, but the proper recommendation for this should be based on research. Proper Se fertilization could enrich the Se level in feedstuffs, which may take care of the Se nutrition in animal feeding in a better way than the current practice of supplementing feed with inorganic Se. This is because the natural organic form of Se has special advantages over the inorganic form as discussed in the paper. An integrated method involving fertilization of soils and fortification of forages can be used to eradicate the deficiencies.

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